REMARKS

The Office Action dated January 9, 2009, has been reviewed, and the comments of the U.S. Patent Office have been considered. Claims 1, 4, 5 and 46 have been amended and claims 7-16, 22-25, 31, 32, 37-42, 44 and 45 are withdrawn from consideration. The amendments do not add new matter. The amendments to Claims 4 and 5 present these claims in independent format, but otherwise, the claims are identical in scope and wording to the same claims as previously presented in dependent format. Claims 1 and 46 have been amended to further indicate that the claimed antibody, by binding to the specific epitope identified, modulates the interaction between human TSG101 and MDM2. This is disclosed throughout the specification, see, e.g., page 2, where it is indicated that such modulation may control ubiquitination within the cell. Indeed, the specification provides specific assays for detecting whether such a targeted antibody does in fact modulate the TSG101/MDM2 interaction – see pages 23 – 32.

REJECTION UNDER 35 U.S.C. § 102(B)

Claims 1, 6, 43, 46, 49 and 50 stand rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by Li et al. (U.S. Patent No. 5,891,668) (hereinafter **Li et al.**). This rejection is respectfully traversed. The traversal is in two parts.

Initially, Applicants note that as to Claims 1, 6 and 43, these claims now require that the antibody bind to the ubiquitination region to an epitope in the region so indicated, but also modulate the interaction between TSG101 and MDM2, an important interaction in cell cycle machinery. It goes without saying that neither **Li et al.**, nor any other reference of record, suggests that an antibody could be prepared directed against ANY epitope which modulates this

important interaction, and thereby modulates ubiquitination. The assay results set forth in the specification make it clear that not ALL antibodies that bind TSG101 in this region modulate that interaction, or otherwise control ubiquitination. Indeed, the reference newly cited by the Office, **Ferrer et al.**, makes the point that antibodies raised against TSG101 that bind in the region of residue 54, will not recognize TSG101, and not modulate the interaction. See the paragraph bridging the columns of page 2257. See also, the discussion on page 2258, which indicates that alone, TSG101 may block ubiquitination, which is essential for cell cycling, and that the antibody-undetected from may not be able to alter ubiquitination regulation.

Accordingly, it is clear that an antibody which modulates the interaction between TSG101 and MDM2 provides a key function, one not inherent in the generic disclosure of **Li et al.**, which indicates in relevant part only that the proline rich domain of TSG101 may be a good target for antibodies as epitopes. Column 8, lines, 64 – Column 9, line 4. Since not all antibodies directed to this region will not modulate the interaction between TSG101 and MDM2, and therefore ubiquitination, these claims are not met.

With respect to Claims 43 and 50, these claims are not so amended, but, it is respectfully submitted are not met by the reference. Both of these claims specifically recite that the antibody is present *together with a pharmaceutically acceptable excipient*. **Li et al.** does not disclose such an excipient. These claims require the excipient or carrier because they are intended as pharmaceutical compositions for the treatment of TSG101 dependent diseases – cancers, viruses, etc. They must be suitable for administration to a mammal, including humans. **Li et al.** simply does not disclose this.

This is specifically because **Li et al.** ascribes to the antibodies generally referred to, but nowhere exemplified, only diagnostic value, to be done *in vitro*. See generally, Column 9, lines 3 – 4 (*Antibodies that recognized TSG101 are useful in diagnosis, typing and staging of human tumors, e.g., carcinomas).* See also Column 9, lines 22 – 42. Nowhere is a pharmaceutical utility described. Instead, other agents, typically small molecules, are identified as satisfactory pharmaceuticals. Column 11, line 45 – Column 12, line 35. Nowhere is a pharmaceutically acceptable composition, that is, one with a pharmaceutically acceptable excipient, comprising an antibody described! These two claims are not met by the reference.

Forestalling a rejection based on the record in another action, the secondary reference applied in support of obviousness claims, **Ferrer et al.**, does not teach antibodies to be useful pharmaceutical agents. It is one thing to say antibodies to TSG101 are known, another to say they are taught to be useful as pharmaceutical agents in a pharmaceutical composition with a pharmaceutically acceptable excipient or carrier. The rejection of these claims is respectfully traversed.

REJECTION UNDER 35 U.S.C. § 103(A)

Claims 4, 5, 47 and 48 stand rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Li et al. in view of Ferrer et al. (Oncogene 1999, 18: 2253-2259) (hereinafter **Ferrer et al.**). This rejection is respectfully traversed.

Li et al. has been discussed above. It discusses three specific domains for epitopes, and in effect teaches specifically away from the claimed invention. For instance, **Li et al.** does not teach that antibodies to any domain of TSG101 would be of value, including e.g., 1 – 140, but

some would be better. It indicates ONLY the three domains. The Examiner notes that **Ferrer et al.** teaches that there is an N-terminus domain in a mutant TSG101 that contains a ubiquitin regulatory region similar to that of normal TSG101, and a leucine zipper different form that of wild-type TSG101. So what? **Ferrer et al.** does NOT teach that either of these regions makes a good target for an antibody. Indeed, this rejection takes nothing from **Ferrer et al.**, it is based SOLELY on the teaching of the art that a mutant TSG101 of unknown character has a region of some homology to the ubiquitination region of TSG101. **But nowhere does this assemblage of art teach the preparation of an antibody that binds in this region. Taking Li et al. and Ferrer et al. together, one is left still with the teaching of Li et al. that one prepares an antibody directed to the proline rich, leucine zipper or coiled coil domains. None of these are embraced by the claims.**

Why would one of skill in the art go against the teaching of **Li et al.**? This the action does not explain. Some powerful teaching away is required, to support the rejection, and none is presented. The Examiner's citation of *Ex parte Erlich* and *Ex parte Sugimoto* is noted but not understood. It is agreed that by Applicants' filing date, January 19, 2001, TSG101 had been purified and identified. So what – Applicants are not CLAIMING an antibody to TSG101. Indeed, these same Applicants are named inventors on an earlier case where that specific subject matter has been claimed. Applicants are claiming antibodies directed to a very specific part of that protein, a part not only not identified as of interest or antigenic or valuable as an epitope, but in fact taught away from as an epitope. The only thing **Ferrer et al.** has to say about antibodies to TSG101 is that an antibody directed to an epitope of unknown character, involving residues 136 – 374, again, away from the claimed invention, doesn't work. (Note that **Ferrer et al.** also

teaches that "the available antibody" to TSG101 at the time of the invention binds in the region of 135 – 374…not the claimed region.

In view of the foregoing, the rejection for obviousness is respectfully traversed, and withdrawal is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this Application and the prompt allowance of at least Claims 1, 4-6, 43 and 46 – 50.

Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 10-0233. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

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Respectfully submitted,

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